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K&L Gates LLP
P.O. Box 1135
CHICAGO, IL 60690

| EXAMINER | |
|---|---|
| EBRAHIM, NABILA G | |
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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 10/089,658
Filing Date: July 22, 2002
Appellant(s): BERGER ET AL.

Robert Barrett
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 11/25/2008 appealing from the Office action mailed 3/25/2008.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

Di Marzo V. 2-Arachidonoyl-glycerol as an "endocannabinoid": limelight for a formerly neglected metabolite, Biochemistry (Mosc). 1998 Jan;63(1):13-21.

| | | |
|---|---|---|
| 6552031 | Burch et al. | 4-2003 |
| WO9428913 | Kyle et al. | 12-1994 |

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

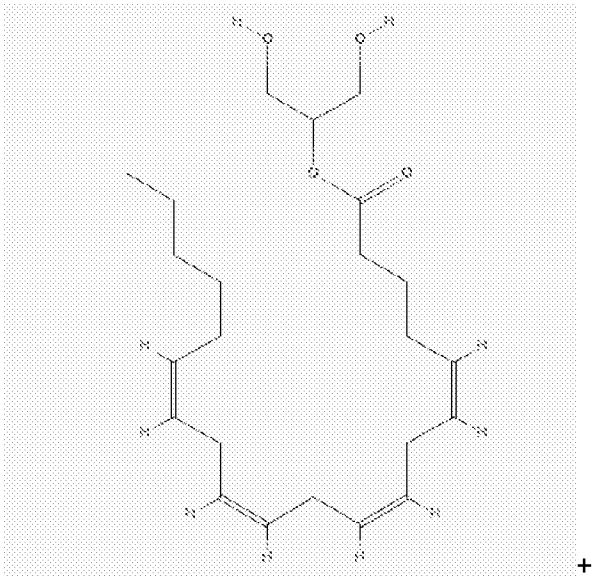
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1, 3-11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Marzo V. 2-Arachidonoyl-glycerol as an "endocannabinoid": limelight for a formerly neglected metabolite, Biochemistry (Mosc). 1998 Jan;63(1):13-21 (hereinafter Marzo) in view of Burch et al. US 6552031 (hereinafter Burch)

Marzo teaches that alternative precursor for arachidonic acid, 2-arachidonoyl-glycerol has cannabimimetic activity. In addition, Marzo discloses that a composition comprising the precursor of arachidonic acid have led to the proposition of a role of the monoglyceride as an "endocannabinoid", starting from its newly discovered pharmacological properties in both central and peripheral tissues and ending with studies on the possible biosynthetic pathways for its formation. Also considered are possible interactions with another arachidonic acid-derived endogenous cannabinoid, anandamide.



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The reference discloses the importance of the same sterochemical configuration of AarG which is diglycerides bearing AA in *sn*-2 position. AArG precursors for 2-AG may be formed from the enzymatic hydrolysis of *sn*-2-AA-containing phosphatidic acid (PA) coming also from the PLD-mediated conversion of N-ArPE into ANA. Again, in this case the two "endocannabinoids" may be produced simultaneously (see page 6 and Fig. 3). Marzo also recognized the palmitoylethanolamide and leamide in the process of detecting the importance of anandamide precursors as agonist for cannabinoid receptors (see page 3). Arachidonic acid is known to be naturally occurring in dietary animal source.

Marzo did not disclose a combination of an anandamide precursor and NSAID.

Burch teaches that combinations of analgesic drugs cause synergism of its analgesic effect. Burch exemplifies the combinations by using oxycodone and NSAID's (rofecoxib).

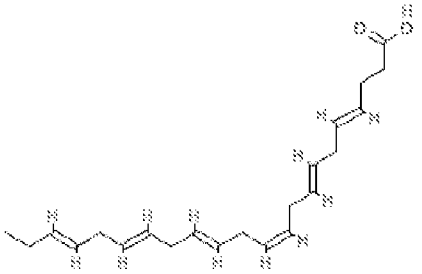
It would have been obvious to a person having ordinary skill in the art at the time the invention was made to combine an anandamide and/or an anandamide precursor with NSAID's to enhance the analgesic effect of both drugs. It would also be a good motivation to the skilled artisan to replace oxycodone with anandamide as anandamide derivatives and precursors do not have the addictive characteristics of oxycodone. The ordinary skilled person would have expectations of success since NSAID's have been combined with other analgesic drugs successfully and enhanced the effect of analgesia for the patients.

2. Claim 14-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Marzo V. 2-Arachidonoyl-glycerol as an "endocannabinoid": limelight for a formerly neglected metabolite, Biochemistry (Mosc). 1998 Jan;63(1):13-21 (hereinafter Marzo) in view of Burch et al. US 6552031 (hereinafter Burch) and further in view of Kyle et al WO 94/28913, the reference is provide by applicant in the IDS dated 3/28/2002 (hereinafter Kyle).

Marzo in view of Burch has been discussed supra.

Both references do not teach a therapeutic composition for oral administration. In addition, the reference is deficient in disclosing manufacturing the therapeutic or the nutrient.

Kyle discloses a method of treating patients suffering from neuro-degenerative ailments associated with DHA or arachidonate (ARA) deficiency (abstract and page 6 lines 10-30, continuing to page 7 lines 1-6).



CID: 6433873

NLM Toxicology: Link

Substance: 1 Link

Related Compounds:
Same, Connectivity: 8 Links
Same, Isotopes: 7 Links

Similar Compounds: 83 Links

Structure Search

Medical Subject Annotations: (Total:1)

Docosahexaenoic Acids
C22-unsaturated fatty acids found predominantly in FISH OILS.

Further, the method includes treating neurological disorders, such as neurodegenerative diseases and psychiatric disorders, by administering a composition comprising a therapeutically effective amount of a single cell microbial oil comprising docosahexaenoic acid (DHA), a single cell oil comprising arachidonic acid (ARA) or a combination of DHA- and ARA-containing oils, to a person in need of such treatment. The oils can be administered as a pharmaceutical composition, a dietary supplement, or in the form of a food product by replacing a portion of the vegetable oil or fat thereon. The preparation method includes purifying the oil and extracting (which is equivalent to the synthesizing step), see pages 16 and 17.

Accordingly, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to purify the naturally occurring arachidonic acid derivative disclosed by Marzo or use the ARA disclosed by Kyle to treat different disorders expanding

those disclosed by the Kyle and make an oral therapeutic product as disclosed by Kyle to advance the treatment of these ailments and facilitate to patients taking their therapeutic needs in an easy oral dosage form or nutrient.

**(10) Response to Argument**

**Appellant argues that:**

- There exists no reason why the skilled artisan would combine Di Matzo and Burch to arrive at the present claims since oxycodone and anandamide have different mechanism of action and because the Patent Office admits that Di Matzo does not disclose a combination of an anandamide precursor and an NSAID, the Patent Office cited Burch to cure the deficiencies of Di Matzo.

**To respond**: Burch teaches generally that combinations of analgesic drugs cause synergism of its analgesic effect. Burch exemplifies the combinations by using oxycodone and NSAID's (rofecoxib). The different mechanisms of action between oxycodone and anandamide which appellant explains in detail is not a concern in such combination, however, the combination of NSAID's and oxycodone or anandamide is the real concern and such combinations (NSAID's/oxycodone or NSAID's/anandamide) wherein oxycodone and anandamide are having different mechanisms of action form NSAID's are known to enhance synergism since two different receptors work on different paths to perform the same effect. It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine an anandamide and/or an anandamide precursor with NSAID's to enhance the analgesic effect of both drugs. It would also be a good motivation to the skilled artisan to replace oxycodone with anandamide because anandamide derivatives and precursors do not have the addictive characteristics of oxycodone.

- Burch teaches the combination of oxycodone and rofecoxib. However, Applicants submit that, in contrast to the Patent Office's assertion, the skilled artisan would have no reason to replace oxycodone with anandamide to arrive at the present claims because opioid analgetics, such as oxycodone, may be deployed as a substitute for heroin or morphine, and can results in similar negative side-effects. For example, opioid analgetics can be extremely addictive to the user and can result in adverse reactions including respiratory depression, orthostatic hypotention, hallucinations, hyperalgesia, delirium, etc.

**To respond:** The office action was clear regarding addictive effect of oxycodone and expresses clearly that this is a good motivation to a person having ordinary skill in the art to replace oxycodone with an anandamide precursor to avoid addiction and side effects in addition to establishing the disclosure of Burch that combinations of analgesic drugs cause synergism of its analgesic effects. Note that Burch did not specify a combination of analgesics comprising narcotic analgesics but generalized the disclosure to encompass all analgesic drugs.

- Regarding claims 14-25, applicant argues that Kyle merely specifies the use of non-modified polyunsaturated acids like DHA or ARA. See, Kyle, Abstract. The Examiner has applied hindsight reasoning by attempting to selectively piece together teachings of each of the references in an attempt to recreate what the claimed invention discloses.

**To respond:** ARA is one of the compounds comprised by the precursor in the Markush group recited in the instant claims wherein the structure includes 20-carbon chain and four *cis* double bonds; the first double bond is located at the sixth carbon from the omega end as recited in the claims. Regarding hindsight, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's

disclosure, such a reconstruction is proper. In the instant case, Marzo teaches that alternative precursor for arachidonic acid, 2-arachidonoyl-glycerol has cannabimimetic activity. Burch teaches that combinations of analgesic drugs cause synergism of its analgesic effect and finally, Kyle discloses the method of treating patients suffering from neuro-degenerative ailments associated with DHA or arachidonate (ARA) deficiency. Kyle also teaches that the preparation method includes purifying the oil and extracting (which is equivalent to the synthesizing step). Note that these are the only two steps recited in the claims beside obtaining and administering.

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Nabila G Ebrahim/

Examiner, Art Unit 1618

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617